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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Paper No. 20

Serial Number: 08/105444
Filing Date: 8/11/93
Appellant(s): Lynn E. Spitler

Kate H. Murashige
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 12/11/95 (Paper No. 19).

The text of those sections of Title 35 U.S.Code not included in this appeal can be found in a previous Office action herein.

(1) Status of Claims.

The statement of the status of claims contained in the brief is correct.

This appeal involves claims 1-40.

(2) Status of Amendments After Final.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(3) Summary of Invention.

The summary of invention contained in the brief is correct.

(4) Issues.

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows:

Issue 1. Appellant states that the issue is whether it is mandatory to include in vivo clinical data in order to support claims to methods of inducing an antitumor immune response and to compositions for this purpose, as set forth in the rejection of the claims under 35 U.S.C. § 112, first paragraph.

In contrast, the examiner has maintained the rejection under 35 U.S.C. § 112, first paragraph in view of the Forman factors. Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

Appellant's intended and claimed invention is drawn to anti-prostatic cancer methods and vaccines. A vaccine must by definition provide an immunoprotective response upon administration.

Issues 2 and 3 are correct.

Issue 4. Upon reconsideration, the previous rejection of claims 1-40 under 35 U.S.C. § 103 has been withdrawn in response to a lack of motivation by the references of record to treat prostate cancer via vaccination rather than targeting with immunotoxins, chemotherapy and surgery. Although newly cited art indicates that attempts to vaccinate against prostatic cancer with prostate-specific tissue was known at the time the invention was made; this same art further supports the examiner's rejection of record under 35 U.S.C. § 112, first paragraph, by indicating the lack of predictability of inducing an effective anti-prostate tumor response (Hodge et al. Int. J. Cancer, 1995).

(5) Grouping of Claims.

With respect to Issues Nos. 1 and 3; the rejection of claims 1-40 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.162(c)(5).

The appellant's statement in the brief that certain claims do not stand or fall together is agreed with respect to Issue No. 2. Therefore, Issue No. 2 is not applicable to claims 3, 9, 16, 23, 29 and 36.

Since the previous rejection of claims 1-40 under 35 U.S.C. § 103 has been withdrawn, appellant's comments are deemed moot.

(6) Claims Appealed.

A substantially correct copy of appealed claim 16 appears on pages 1-7 of the Appendix to the appellant's brief. The minor error is as follows. Claim 16, line 2 is objected to because "speicific" should be "specific".

(7) Prior Art of Record.

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

1) Ezzell, J. NIH Research 7: 46-49, 1995.
2) Deguchi et al., Cancer Res. 45: 3751-3755, 1986.
3) Chu et al., U.S. Patent No. 4,446,122, 5/1/84.

(8) New Art.

Spitler (instant inventor) and Hodge et al. have been applied in response to appellant's arguments indicating examiner's reliance on scientific reasoning relating to routine clinical problems and examiner's lack of support addressing the problem that the invention purports to solve.

1) Spitler, Cancer Biotherapy 10: 1-3, 1995.
2) Hodge et al. Int. J. Cancer 63: 231-237, 1995.

(9) Grounds of Rejection.

The following ground(s) of rejection are applicable to the appealed claims.

Rejection Under 35 U.S.C. § 112, First Paragraph

Issue 1. Antitumor methods and vaccines.

The specification is objected to and claims 1-40 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. In evaluating the facts of the instant case, the following is noted:

Appellant has not enabled the breadth of the claimed invention in view of the teachings of the specification. Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

Appellant has not disclosed how to use the claimed vaccines and methods to treat prostatic cancer as a therapeutic regimen in humans. There is insufficient evidence of the invention with respect to the in vivo operability of the claimed prostate-specific proteins, peptides or fragments thereof as well as anti-idiotypic antibodies to use appellant's invention.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Concerning vaccines in general, the antigenic or immunogenic nature of a protein or an anti-idiotypic antibody does not necessarily correlate with its ability to confer protective efficacy as a vaccine. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

As disclosed on page 2, paragraph 1 of the instant specification; appellant discloses that prostate cancer continues to be refractory to treatment despite many years of efforts to improve therapy. Similarly, appellant discloses that vaccine development has been slow and no vaccine approved by the FDA for marketing currently exists for any form of cancer. Appellant has not provided any evidence a priori that establishes the efficacy of the instant invention drawn to an antigen (e.g. protein, peptide or fragment thereof) overrepresented in the prostate gland (e.g. PSA, PSMA or PAP) for the treatment of human prostatic cancer.

In the instant application where the prostate gland itself is not eliminated, the claimed therapeutic methods and vaccines could lead to other problems in the host by eliciting prostate specific immunity. The generation of an immune response against self even if it is against tissue-specific antigens could elaborate into an autoimmune response against other antigens (e.g cross-reactive antigens) of the host.

No examples or nexus is provided in the application of prostate-specific antigen-mediated therapy as a therapeutic regimen for human prostate cancer.

In view of the lack of predictability of the art to which the invention pertains and the lack of established clinical protocols for effective cancer vaccines and prostate cancer therapies; undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and compositions and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for establishing protective antitumor responses.

Issue 2. Scope of overrepresented prostate antigens.

Appellant discloses that the antigens overrepresented on prostate includes any other antigens substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissues by virtue of the presence of these antigens (see pages 9-10). There is no evidence relating to overrepresented prostate-specific antigens other than PSA, PSMA and PAP to practice all of the claims vaccine compositions and methods embraced by the claims. The specification has not provided sufficient direction or guidance to one of skill in the art to properly select prostate antigens other than PSA, PSMA that are required to enable the broadly claimed compositions and methods. It appears that undue experimentation would be required of one skilled in the art to practice the broadly claimed

compositions and methods using the teaching of the specification alone.

Appellant relies on the specification's adequate teaching concerning the appropriateness of any antigen overrepresented on prostate tissue. The specification is written in terms of an antigen that is "sufficiently higher" in the prostate over other tissues and of an immune response that results in "relatively sparing of other organs and tissues" (page 5, paragraph 2). In consideration with the lack or predictability concerning cancer vaccines, it would be undue experimentation to investigate all the possible variations of possible immunogens that may result in an appropriate prostatic cancer vaccine. Appellant has not enabled a prostatic cancer vaccine based on PSA, PSMA or PAP, which are known prostatic antigens; as indicated above in section A. It would be even less predictable to provide an appropriate prostatic cancer vaccine based on overrepresented prostatic antigens not even known yet. Just because an antigen may be overrepresented, it does not make it a suitable vaccine candidate. Just because an antigen can be made immunogenic, it does not make it a suitable vaccine candidate.

Issue 3. Scope of antigens, fragments and portions.

Claims 1-40 are not enabled for the breadth of "at least one/an antigen overrepresented in the prostate gland", "immunologically effective portion thereof", "exhibits posttranslational modification different from those of PSA produced in human cells", "immunologically effective portion" and "ingredients which are active to elicit said immune response". The characteristics of these antigens are not clearly defined and encompasses potentially thousands of different proteins or peptides. The specification fails to provide sufficient guidance as to how to determine all such proteins and peptides. It would require undue experimentation to produce all such possible proteins and peptides without more explicit guidance from the disclosure.

The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. Ezzell reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (J. NIH Research, 1995; see entire document, particularly the last paragraph). It is well known in the art that tumor cells in vivo simply do not display their unique antigens in ways that are easily recognized by cytotoxic T lymphocytes (Ezzell; page 48, column 2, paragraph 2). Furthermore, no one is very optimistic that a single peptide or a virus carrying the gene encoding that peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of

micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (Ezzell; page 48, paragraph 6).

No direction or guidance is provided to assist one skilled in the art in the selection of all such possible vaccine derivatives nor is there evidence provided that all such derivatives would be therapeutically effective. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods and compositions in providing effective vaccines for prostatic cancer using the teaching of the specification alone.

(10) Response to Argument

Rejection Under 35 U.S.C. § 112, First Paragraph

Appellant's arguments have been fully considered but are not found convincing.

The scope of the claims must bear a reasonable correlation with the scope of enablement, In re Fisher, 166 USPQ 19 24 (CCPA 1970).

Issue 1. Anti-tumor methods and vaccines.

Appellant relies upon the holding and dicta in In re Brana 34 USPQ2d 1436 (Fed. Cir. 1995) that their position that it is necessary to supply in vivo clinical data to support claims of the type proposed here. Appellant states that the examiner was not correct that in Brana, "animal models were art recognized to be predictive of therapeutic usefulness". However, the examiner's position was that Brana was directed to chemical chemotherapeutic compounds structurally similar to other compounds known in the art and for which animal models were art recognized to be predictive of the therapeutic usefulness and which were, as a class, recognized to be effective in treating tumors (Paper No. 13). The examiner was pointing out that the compounds disclosed in Brana were the same or similar to a class of compounds that were predictive of therapeutic usefulness in animal models and not that animal models per se were predictive of human efficacy.

The examiner agrees that the it is unnecessary that appellant must prove the ultimate value in humans of their asserted utility. The issue in this case is not whether the general description in the specification of utility, practical or otherwise, for a claimed compound reasonably satisfies the utility requirements of 35 U.S.C. 112, first paragraph and 101, as the Court viewed the case in Brana. Rather the issue here is whether appellant's specification which provides no working

examples enables any person skilled in the art to use the full scope of claimed antitumor veterinary and human methods and vaccines which are so broad in scope that they contemplate and encompass every known and unknown overexpressed prostatic antigen or fragment thereof.

The examiner stands corrected that the burden of proof is a preponderance of evidence and not clear and convincing evidence. However, the examiner has set forth a prima facie case of lack of enablement under 112, first paragraph, in view of the Forman factors, which is of record including appellants disclosed admission in the specification.

Appellant appears to dismiss doubts based upon the examiner's scientific reasoning as set forth above including the citation on page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992)(see section 9, Issue 1 above). This citation also appears to be the source of appellant's mischaracterization of the examiner's rejection that in vivo clinical data is required to overcome the rejection of 35 U.S.C. 112, first paragraph rather than examiner's reliance on the Forman factors. The examiner has set forth the art-known problems associated with the unpredictability of therapeutic methods and compositions in the absence of objective evidence or working examples that are reasonably predictive of the scope of the claimed invention. This is not the same as requiring clinical data as asserted by appellant.

Although appellant has provided a general strategy for the claimed antitumor methods and vaccines; due to the unpredictable nature of the art, it does not appear that the general teachings are sufficient to enable the ordinary skilled artisan to either make or use the claimed inventions. Although the presence of working examples is not necessarily a criterion for enablement of the claimed invention, due to unpredictable nature of the art (i.e. cancer vaccines and vaccination), it would require undue experimentation for the ordinary skilled artisan to practice the invention as claimed.

It is not necessary for the examiner to cite published authority to raise doubt. It is necessary only to provide acceptable reasoning. In re Budnick, 537 F.2d 535, 190 USPQ (CCPA 1976).

In an analogous situation of cancer treatment, claims for cancer treatment involving combination therapy using anti-tumor monoclonal antibodies or immunotoxins with interleukin-2 were properly rejected, in view of acknowledged lack of actual evidence as to usefulness of claims and processes for treatment cancer, since mere speculation, or presentation of experimental

"paper" protocol, is not sufficient. Ex parte Stevens 16 USPQ2d 1379 (CPAI 1990).

Suffice it to say that in every cited case the narrow issues involved was whether or not the evidence of record was based on in vivo or in vitro studies which were generally recognized by those of ordinary skill in the art as being reasonably predictive of success in the practical utility under consideration, i.e., human or , at least mammalian therapy. Ex parte Stevens citing Ex parte Busse, 1 USPQ2d 1909 (BPAI 1986).

Appellant argues that the instant invention differs from the lack of predictability referenced by tumor associated antigens and peptides thereof disclosed by Ezzell et al. (J. NIH Research, 1995). Appellant argues that the antigens of the instant invention are also displayed on normal prostate as well as benign/malignant tumor tissue; therefore they do not suffer from the defects characteristic of unique tumor antigens. However, appellant has not provided any objective evidence how single proteins or peptides triggering an immune response strong enough to eradicate tumors or prevent the growth of micrometastases differs between the antigens taught by Ezzell et al. and those encompassed by the claimed inventions.

Also, it is the tissue specificity of an antigen that makes is a potential target antigen for active specific immunotherapy. Therefore instant prostate-specific antigen would not have been considered any different from any other tumor associated antigen targeted in cancer therapy. Therefore, appellant's asserted distinction purported in the instant invention is without foundation. For example, the previous rejection under 35 U.S.C. § 103 relied upon Deguchi et al. (Cancer Res., 1986) and Chu et al. (U.S. Patent No. 4,446,122); both of which teach targeting human prostate tumor with PSA- or PAP-specific immunotoxins. Both prostate-specific antigen specificities are encompassed and recited by the claimed invention. Furthermore, Hodge et al. (Int. J. Cancer, 1995) discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant shown little or no therapeutic benefit (page 231, column 1, first paragraph of Introduction). Here, the reference discloses that these previous attempts to actively immunize were known in 1990, prior to appellant's invention. Such prostate adenocarcinoma cells and normal prostate cells express common antigens. Therefore, targeting prostate-specific antigens that are expressed on both normal and tumor cells in cancer immunotherapy to target tissue-specific antigens was known and practiced at the time the invention was made.

As the instant inventor acknowledges (Spitler, Cancer Biotherapy, 1995; page 1, column 1, paragraph 1); "Ask practicing oncologists what they think about cancer vaccines and you're

likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company, and you're likely to get the same response". Therefore, appellant again recognizes the lack of predictability of the nature of the art and state of the prior art to which the instant invention pertains, as similarly disclosed on page 2 of the specification. Also, such disclosures clearly indicate that the amount of direction or guidance presented in the specification is limited, and would not permit a person skilled in the art to use the invention without undue experimentation at the time the invention was made.

With respect to prostate-specific immunotherapy, Hodge et al. (Int. J. Cancer, 1995) discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant shown little or no therapeutic benefit (page 231, column 1, first paragraph of Introduction). Models of evaluation of prostate therapeutics including the canine and the Dunning rat are not practical for PSA-recombinant vaccines due to the very low homology of rat and canine PSA to human PSA (page 231, column 2, paragraph 2). The fact that human PSA is a secreted antigen should be taken into consideration for its potential use as a target for human prostate cancer, as the secreted antigen may also reduce immunoglobulin responses by forming antigen-antibody complexes and/or potentially anergizing specific T cell responses (page 235, column 1, lines 1-6). An immune reaction directed against PSA could lead to side effects resulting from cross-reactivity with other kallikrein family members (page 235, column 2, lines 4-6). Therefore, the use of prostate-specific antigens in vaccines are likely to be limited by either neutralization by secreted prostate antigen or by inducing autoimmunity. Although the recombinant human PSA construct was unable to elicit an anti-PSA IgG response, PSA-specific IgM response were noted in all immunized monkeys (page 236, column 1, paragraph 1). However, these antibody responses were of low titer, were short-lived and could not be boosted. It is noted that the monkeys developed in vitro lymphoproliferative responses to PSA (page 236, column 1, paragraph 2). However, it is not clear that such studies can be extrapolated to humans because in the difference in MHC motifs between rhesus and humans and the levels of expression of class I and II MHC on rhesus vs. human prostate and human normal prostate vs. prostate carcinoma (page 236, column 2, last paragraph). In addition to these cautions with respect to appropriate antigen presentation and subsequent immune responses (issue of MHC), this reference clearly indicates limited antibody responses and only some level in vitro cellular immunity with prostate specific antigen immunization. Also, this reference clearly indicates the limitations of animal models in prostate cancer modalities and that previous attempts at human prostate cancer vaccination with whole cells.

Therefore, Hodge et al. (Int. J. Cancer, 1995) provides evidence to support the examiner's scientific reasoning of record that indicated the lack of predictability in the absence of evidence to the contrary of appellant's claimed anti-prostate tumor methods and vaccines.

Full enablement of claims on vaccines should include teachings on the relevant immunogenic proteins and portions thereof, the level of neutralizing antibody or cellular immunity produced and the efficacy of the vaccine against subsequent inoculations of the intended pathogen, in this case a prostate tumor. Since the immune response is considered to be one of the most complex and unpredictable biological processes, without any guidance or teachings of any of the above, it is considered that it would require undue experimentation for the ordinary skilled artisan to make or to use the invention as claimed.

Appellant has not provided any in vitro or in vivo correlate for the claimed antitumor methods and vaccines other than the prevention and treatment of prostatic cancer (page 4, paragraph 1 and page 15, paragraph 2 of the specification). It is not clear that the art recognizes such a correlate exists for cancer vaccines. Even though a particular immune response may be elevated (e.g. antibody or cytotoxic T lymphocyte), the skilled artisan would not ascribed in vivo significance to that observation. It is not necessarily true that an epitope or group of epitopes will be a potent tumor vaccine. Although whole cells or cell lysates are crude, and to a limited degree, useful in causing regressions of disease and prolongation of survival in certain cases, it would not be necessarily predictive that single proteins of small peptides thereof would lead to an effective vaccine. In the case of prostate cancer, human prostate cancer vaccination with whole cells has not been successful (Hodge et al., Int. J. Cancer, 1995 cited above); therefore relying on any prostate-specific antigen or fragment thereof would not be predictive in the absence of objective evidence supporting the scope of the claimed invention.

As stated in In re Wright 27 USPQ2d 1510, 1512 (CAFC 1993), the issue is now what the state of the art is today or what a skilled artisan today would believe, but rather what the state of the art at the time of filing and what a skilled artisan would have believed at that time. Hybritech Inc. v. Monoclonal Antibodies, Inc. 802 F2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir.), cert denied, 480 U.S. 947 (1987); In re Hogan, 559 F2d 595, 604, 194 USPQ 527, 535 (CCPA 1977).

Therefore, the record clearly shows that there was lack of predictability of appellants antitumor methods and vaccines including the claimed prostate specificity at the time the invention was made and that this lack of predictability remains current, including the instant inventor's own admission (Spitler, Cancer Biotherapy, 1995).

Issue 2. Scope of overrepresented prostate antigens.

Appellant argues that the inventions resides in the recognition that a host tissue antigen, which antigen is shared with a tumor inhabiting the host tissue, and which antigen distinguishes immunologically the tissue from other types of host normal tissue can be used to elicit an immune response against prostate tumor. Since appellant's invention does not relate to the discovery and description of these antigens but rather to a method of use them once they are discovered; appellant argues that it would be unfair to limit the claims to those prostate-specific antigens that happen to be known at the time the instant inventor's application was written. Appellant argues that this is analogous to claims drafted to expression systems for production of various proteins.

While it would be predictable that a strong or regulated promoter could be used generally in the production of a number of recombinant proteins in expression systems, it is not predictable that a protein or a peptide can elicit an immune strong enough to confer a protective immune response for the reasons set forth above.

More importantly, one cannot make that of which one has no conception. Appellant discloses that the antigens overrepresented on prostate includes any other antigens substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissues by virtue of the presence of these antigens (see pages 9-10).The specification is written in terms of an antigen that is "sufficiently higher" in the prostate over other tissues and of an immune response that results in "relatively sparing of other organs and tissues". In turn, the claims generically encompass potentially a number of prostate antigens that are not defined structurally and biologically to a very limited degree.

In contrast to appellant's asserted analogy; the instant case is more analogous as that found in Amgen v. Chugai, 18 USPQ 2d 1017 at 1021, that: "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See Oka, 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method or preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having nor more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated." Thus, the instant specification does not adequately describe, and therefore cannot adequately teach how to make, the claimed invention.

Similar to the situation in Ex parte Maizel (27 USPQ2d 1662 at 1665 in which it was found that: "Appellants' is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, or a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in In re Hyatt, 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

In addition, an analogous situation can be ascribed to In re Wright 27 USPQ2d 1510, 1512 (CAFC 1993). The Board found that, even if Wright(applicant) was correct in stating that it was generally known that an immune response is assured by use of an antigenic envelope protein, the record did not establish that such an immune response would have been an immunoprotective one, or moreover, that one skilled in this art would have expected such a result in February of 1983. the Board relied upon the Matthew et al. article, as evidence that the mere use of an envelope protein gene in the present invention is not seen to necessarily result in the obtention of successful vaccines throughout the scope of even these more limited claims.

In the instant case not only is the disclosure not commensurate in scope with the claims, the disclosure fails to present even a single operable species of the claimed invention.

In consideration with the lack or predictability concerning cancer vaccines, it would be undue experimentation to investigate all the possible variations of possible immunogens that may result in an appropriate prostatic cancer vaccine. Applicant has not enabled a prostatic cancer vaccine based on PSA, PSMA or PAP, which are known prostatic antigens; as indicated above in section A. It would be even less predictable to provide an appropriate prostatic cancer vaccine based on overrepresented prostatic antigens not even known yet. Just because an antigen may be overrepresented, it does not make it a suitable vaccine candidate. Just because an antigen can be made immunogenic, it does not make it a suitable vaccine candidate.

In analogizing cancer vaccines to interferon, Spitler also discloses the importance in identifying cloning and purifying interferons in advancing interferon-based therapies (Cancer biotherapy, 1996; page 1, column 2, paragraph 1) and that similar identification and characterization is required of cancer vaccines (page 2, column 1, paragraph 1). Spitler concludes that active components of vaccines have been identified and purified, therefore the decade of the vaccines may finally have arrived (page 2, column 2, paragraph 3). Therefore, the instant inventor clearly recognizes the importance of identifying and characterizing potential vaccine candidates rather than relying upon some general feature or biological property such as encompassed by appellant's claimed property of "overexpression".

There is no disclosure of the complete amino acid sequence of any protein, nor is there any disclosure of even a single peptide that would meet the limitations of the claims. Thus, there is no teaching of structure that the artisan could use as a guide in making the claimed overrepresented prostate antigens or fragments thereof. In the absence of any working examples, any guidance as to the structure of the claimed overrepresented prostate antigens and fragments thereof, and the unpredictability inherent in making anti-tumor vaccines, it would require undue experimentation to practice the claimed invention by relying on properties defined almost solely by function.

Issue 3. Scope of antigens, fragments and portions.

In section C on pages 8-9 of the Brief, appellant indicates that the examiner states, "while the examiner acknowledges that the various fragments forms claimed can elicit an immune response, applicant's invention ..." and no further comment is made. Therefore appellant's arguments focuses on only the "immunologically effective portions" aspect of the rejection and assumes the objections to the terms :at least one antigen overrepresented in the prostate gland, peptide and exhibits posttranslational modification different from those of PSA produced in human cells" mentioned in the rejection under 35 U.S.C. § 112, first and second paragraphs.

The following paragraph is a reiteration of the examiner's position set forth in Paper No. 12, mailed 8/15/95.

Upon reconsideration and in view of applicant's arguments, filed 7/10/95 (Paper No. 11); the previous rejection of claims 1-40 under 35 U.S.C. § 112, first and second paragraphs, is withdrawn with respect to the second paragraph aspect of this rejection. However the rejection of claims 1-40 under 35 U.S.C. § 112, first paragraphs are maintained for the reasons of record, set forth in the Office Action, mailed 3/7/95 (Paper No. 9). While the examiner acknowledges that the various fragment forms claimed can elicit an immune response; applicant's invention is drawn to eliciting an anti-tumor response with the aspect of being a vaccine. Eliciting an immune response and eliciting an effective anti-tumor response are not the same. As of record, Ezzell (J. NIH Research, 1995), no one is very optimistic that a single peptide or a virus carrying the gene encoding that peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (page 48, paragraph 6).

Therefore, the examiner had withdrawn the second paragraph aspect of the previous rejection of claims 1-40 under 35 U.S.C. § 112, first and second paragraphs. Appellant's assertions of withdrawing 35 U.S.C. § 112, first and second paragraphs, against the other claimed phrases in "quotations" is not correct and it is not clear why appellant assumed this to be the case.

However, appellant's arguments would appear to be the same for these other phrases in quotations as well. Appellant's arguments are essentially a reiteration of appellant's response to the examiner's rejection under 35 U.S.C. § 112, first paragraph, with respect to the complete antigen. Appellant's arguments and the examiner's rebuttal are set forth above in Issues 1 and 2 above.

Again, appellant argues that the antigens of the instant invention are designed to overcome the problems associated with antigens unique to tumor tissue. For the reasons set forth above in Issues I and 2; the art does not recognize this asserted distinction between devising vaccines based on tumor antigens or prostate antigens. In addition, the lack of predictability of anti-tumor methods and vaccines applies to whole antigens and fragments thereof and prostate antigens as well as any other antigen targeted in a vaccine.

Appellant is reminded that the invention is drawn to eliciting an effective anti-prostatic tumor immune response. The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. The references cited above including Ezzell (J. NIH Research, 1995) as well as the instant inventor all agree on the lack of predictability in cancer vaccines. No clear guidance as to the metes and bounds of the various claimed limitations has been provided other than that they should be immunogenic. However, appellant is claiming a universe of antigens yet it is unclear whether any overrepresented prostatic antigen or fragment thereof would provide the appropriate vaccine preparation. In turn, it is not clear whether any portion of any of these overrepresented prostatic antigens would stimulate an effective vaccination. It is clear that the art recognizes that a single peptide is not likely to provide an effective vaccine. Again, just because an antigen (or portion thereof) is immunogenic, this does not make it effective as a vaccine. There are no adequate working examples to indicate that any immunogenic portion of any overrepresented prostate antigen or portion thereof would provide an effective vaccine.

Conclusion.

Appellant's arguments have not been found persuasive and the rejections are maintained.

(11) Period of Response to New Ground of Rejection

In view of the new art cited, appellant is given a period of TWO MONTHS from the mailing date of this examiner's answer within which to file a reply to any new ground of rejection. Such reply may include any amendment or material appropriate to the new ground of rejection. Prosecution otherwise remains closed. Failure to respond to the new ground of rejection will result in dismissal of the appeal of the claims so rejected.

(12) For the above reasons, it is believed that the rejections should be sustained.

Respectively submitted,

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April 25, 1996